PATENT

Attorney Docket No. 003300-589

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	**BOX PCT**
	)	
Ulf Lindahl and Jin-ping Li	)	Attn: DO/EO/US
	)	
Serial No. (corresponds to PCT/SE98/00703)	)	
	)	
Filed: October 18, 1999	)	Group Art Unit: Unassigned
	)	
For: DNA SEQUENCE CODING FOR A MAMMALIAN GLUCURONYL C5-EPIMERASE AND A PROCESS FOR ITS PRODUCTION	)	Examiner: Unassigned

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231
Sir:

This application corresponds to PCT/SE98/00703.

It is contemplated that this Application be prosecuted using Claims 1 to 8 as submitted on May 25, 1999 during the international phase of prosecution and as further herein.

Please amend the above-identified Application as indicated.

In the Abstract of the Disclosure

Please add the Abstract of the Disclosure that is provided herewith on a separate sheet.

In the Claims

Claim 4, line 3, delete "any one of the preceding claims" and insert --claim 1--.

Claim 6, line 2, delete "or 5".

Claim 7, line 6, delete "or 5".

AWAPATENT

Response to Written Opin

Handläggare	Stockholm	Referens
Marie-Louise Ebbinghaus/LFG	1999-05-25	PC-2988293

Ansökningsnr	Rotel	Mål nr
SE98/00703		

PATENT- OCH REGISTRERINGSVERKET
STOCKHOLM

With reference to the written opinion, dated 17-03-1999, a new set of claims is filed and the following is stated:

In the new set of claims, claim 1 has been supplemented with the sequence information from former claim 2. Former claim 2 has been deleted. A new claim 5 has been added. Basis for this claim can be found e.g. on page 9, lines 26- p. 10, line 25. In claim 7 the expression cell line has been substituted with host cell. Basis for that can be found in the examples.

The present invention relates to an isolated or recombinant DNA sequence coding for a glucuronyl C5-epimerase. The DNA sequence is identified in the sequence listing.

In the written opinion documents A and B is cited. Document A relates to a purified bovine enzyme D-glucuronyl C-5 epimerase. Document B discloses the use of a C5-epimerase for the production of polysaccharides with a high iduronic acid content. No document has been found relating to an isolated DNA sequence coding for the enzyme.

The problem behind the present invention was to obtain a method to produce the known enzyme glucuronyl C5-epimerase by a recombinant technique. There are considerable advan-

Bilagor
New claims 1-8

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tages with a recombinant production of this enzyme. Such a produced enzyme is absolutely safe, without any risk of being contaminated by viruses, bacteria, prion protein or any other animal related diseases. There is always such a risk with enzymes produced with conventional methods. Further, the recombinant technique offers an unlimited source of the enzyme of specified quality. The production of large quantities of the enzyme of specified quality would not be possible by using bovine or other animal organs as a source. The use of the recombinant technique can be considered as a prerequisite for industrial scale production of the enzyme. The problem behind the invention was solved by the DNA sequence as claimed in the claims.

According to the written opinion it is not regarded to involve an inventive step to derive the DNA sequence from a known purified enzyme, as long as it has not been shown that the claimed enzyme has any new and unexpected characteristics compared to the known enzyme.

In the present invention the obtained knowledge of the DNA sequence for the known enzyme is the result of several years of qualified work where the successful outcome was not at all given. When finally the DNA sequence was established it was found that the known, earlier isolated enzyme (from document A) was a truncated form of the enzyme which missed 73 amino acid residues in the N-terminal. The full length protein contains two cysteine residues. Cysteine residues often result in di-sulfide bridges in proteins, which usually are important for the function of the protein. It was found that one of these cysteine residues was missing in the enzyme from document A. Still the enzyme was active.

When the DNA sequence for the enzyme had been established there was still the problem to obtain a functional protein with enzyme activity. A great number of experiments were conducted to express the protein in various mammalian cell systems. However, no enzyme activity could be detected. Expression of the enzyme in bacterial systems gave large amounts of the protein but these proteins were also inactive. Finally when the enzyme was expressed in the Baculuvirus system an active enzyme was obtained.

Based on the enclosed claims, where claim 1 has been restricted to the DNA sequence as cited in the sequence listing, it can be stated that all claims are novel compared to the cited state of the art. Further, it can not be regarded as obvious to determine the DNA sequence for the full length protein and also to be able to produce a protein with enzyme activity (i.e. a protein with the correct configuration), when the state of the art only shows a truncated protein with no sequence information at all.

With reference to what has been stated above and based on the enclosed claims, a positive examination report is respectfully solicited.

Ombud **AWAPATENT AB**